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New insights into the neural network of the nongravid uterus

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Abstract

The human uterus is exposed to epigenetic factors during maturation, which might influence its neural network. The mesh muscle is formed from the circular muscle during development and maturation, and it coordinates the longitudinal and circular muscle function. The uterus has an autonomous neural network with contractility and propagation patterns that determine its reproductive potential and health during pregnancy and delivery. Emerging knowledge on the uterine neural network and mesh muscle ultrastructure contributes to new ideas and solutions on the role of intrauterine pressure and distending fluid intravasation during hysteroscopy, and even allows for improving the operative techniques of myomectomy, adenoma cytorreductive surgery and metroplasty. Good health and well-being start from the in utero stage of life. Prenatal and antenatal care are of paramount importance to minimize the risks of malnutrition and pollutants, and foster a healthy uterus. Research regarding the neural network, function and contractility of the nongravid uterus is a new chapter in gynecology that provides significant information for a better understanding and early diagnosis and treatment of uterine pathologies and early pregnancy support.

Keywords: estrogen; myometrium; neurotransmitter; progesterone; uterus.



Forces Involved with Labor and Delivery-A Biomechanical Perspective

Grimm MJ.

Ann Biomed 2021 Aug;49(8):1819-1835. doi: [10.1007/s10439-020-02718-3](https://doi.org/10.1007/s10439-020-02718-3). Epub 2021 Jan 11. PMID: 33432512

Abstract

Childbirth is a primarily biomechanical process of physiology, and one that engineers have recently begun to address in a broader fashion. Computational models are being developed to address the biomechanical effects of parturition on both maternal and fetal tissues. Experimental research is being conducted to understand how maternal tissues adapt to intrauterine forces near the onset of labor. All of this research requires an understanding of the forces that are developed through maternal efforts-both uterine contractions and semi-voluntary pushing-and that can be applied by the clinician to assist with the delivery. This work reviews the current state of knowledge regarding forces of labor and delivery, with a focus on macro-level biomechanics.

Keywords: Biomechanics; Birth.



Efficacy of pediatric integrative manual therapy in positional plagiocephaly: a randomized controlled trial

Pastor-Pons I, Lucha-López MO, Barrau-Lalmolda M, Rodes-Pastor I, Rodríguez-Fernández ÁL, Hidalgo-García C, Tricás-Moreno JM.

Ital J Pediatr 2021 Jun 5;47(1):132. doi: [10.1186/s13052-021-01079-4](https://doi.org/10.1186/s13052-021-01079-4). PMID: 34090515; PMCID: PMC8180102.

Abstract

Background: Positional plagiocephaly frequently affects healthy babies. It is hypothesized that manual therapy tailored to pediatrics is more effective in improving plagiocephalic cranial asymmetry than just repositioning and sensory and motor stimulation. **Methods:** Thirty-four neurologically healthy subjects aged less than 28 weeks old with a difference of at least 5 mm between cranial diagonal diameters were randomly distributed into 2 groups. For 10 weeks, the pediatric integrative manual therapy (PIMT) group received manual therapy plus a caregiver education program, while the controls received the same education program exclusively. Cranial shape was evaluated using anthropometry; cranial index (CI) and cranial vault asymmetry index (CVAI) were calculated. Parental perception of change was assessed using a visual analogue scale (-10 cm to +10 cm). **Results:** CVAI presented a greater decrease in PIMT group: $3.72 \pm 1.40\%$ compared with $0.34 \pm 1.72\%$ in the control group ($p = 0.000$). CI did not present significant differences between groups. Manual therapy led to a more positive parental perception of cranial changes (manual therapy: 6.66 ± 2.07 cm; control: 4.25 ± 2.31 cm; $p = 0.004$). **Conclusion:** Manual therapy plus a caregiver education program improved CVAI and led to parental satisfaction more effectively than solely a caregiver education program.

Trial registration number: NCT03659032; registration date: September 1, 2018. Retrospectively registered.

Keywords: Positional Plagiocephaly, Deformational Plagiocephaly, Manual therapy, Physical therapy

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8180102/>

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Effects of an Exercise Program on Brain Health Outcomes for Children With Overweight or Obesity: The ActiveBrains

Ortega FB, Mora-Gonzalez J, Cadenas-Sanchez C, et al.

Randomized Clinical Trial. *JAMA Netw Open.* 2022;5(8):e2227893. doi: [10.1001/jamanetworkopen.2022.27893](https://doi.org/10.1001/jamanetworkopen.2022.27893).

Key Points

Question: Can an exercise intervention of aerobic plus resistance training improve cognitive and brain health outcomes for children with overweight or obesity? **Findings:** In this randomized clinical trial of 109 participants, exercise significantly improved intelligence and cognitive flexibility among preadolescent children with overweight or obesity. There was also a positive, smaller-magnitude significant effect of exercise on academic performance but no significant effect on inhibition and working memory or on structural and functional brain outcomes studied.

Meaning: This study suggests that exercise can positively affect intelligence and cognitive flexibility during a sensitive period of brain development in childhood and, to a smaller extent, academic performance, indicating that an active lifestyle before puberty may lead to more successful life trajectories.

Abstract

Importance: Pediatric overweight and obesity are highly prevalent across the world, with implications for poorer cognitive and brain health. Exercise might potentially attenuate these adverse consequences. **Objectives:** To investigate the effects of an exercise program on brain health indicators, including intelligence, executive function, academic performance, and brain outcomes, among children with overweight or obesity and to explore potential mediators and moderators of the main effects of exercise. **Design, Setting, and Participants:** All preexercise and postexercise data for this 20-week randomized clinical trial of 109 children aged 8 to 11 years with overweight or obesity were collected from November 21, 2014, to June 30, 2016, with neuroimaging data processing and analyses conducted between June 1, 2017, and December 20, 2021. All 109 children were included in the intention-to-treat analyses; 90 children (82.6%) completed the postexercise evaluation and attended 70% or more of the recommended exercise sessions and were included in per-protocol analyses. **Interventions:** All participants received lifestyle recommendations. The control group continued their usual routines, whereas the exercise group attended a minimum of 3 supervised 90-minute sessions per week in an out-of-school setting. **Main Outcomes and Measures:** Intelligence, executive function (cognitive flexibility, inhibition, and working memory), and academic performance were assessed with standardized tests, and hippocampal volume was measured with magnetic resonance imaging. **Results:** The 109 participants included 45 girls (41.3%); participants had a mean (SD) body mass index of 26.8 (3.6) and a mean (SD) age of 10.0 (1.1) years at baseline. In per-protocol analyses, the exercise intervention improved crystallized intelligence, with the exercise group improving from before exercise to after exercise (mean z score, 0.62 [95% CI, 0.44-0.80]) compared with the control group (mean z score, -0.10 [95% CI, -0.28 to 0.09]; difference between groups, 0.72 SDs [95% CI, 0.46-0.97]; $P < .001$). Total intelligence also improved significantly more in the exercise group (mean z score, 0.69 [95% CI, 0.48-0.89]) than in the control group (mean z score, 0.07 [95% CI, -0.14 to 0.28]; difference between groups, 0.62 SDs [95% CI, 0.31-0.91]; $P < .001$). Exercise also positively affected a composite score of cognitive flexibility (mean z score: exercise group, 0.25 [95% CI, 0.05-0.44]; control group, -0.17 [95% CI, -0.39 to 0.04]; difference between groups, 0.42 SDs [95% CI, 0.13-0.71]; $P = .005$). These main effects were consistent in intention-to-treat analyses and after multiple-testing correction. There was a positive, small-magnitude effect of exercise on total academic performance (mean z score: exercise group, 0.31 [95% CI, 0.18-0.44]; control group, 0.10 [95% CI, -0.04 to 0.24]; difference between groups, 0.21 SDs [95% CI, 0.01-0.40]; $P = .03$), which was partially mediated by cognitive flexibility. Inhibition, working memory, hippocampal volume, and other brain magnetic resonance imaging outcomes studied were not affected by the exercise program. The intervention increased cardiorespiratory fitness performance as indicated by longer treadmill time to exhaustion (mean z score: exercise group, 0.54 [95% CI, 0.27-0.82]; control group, 0.13 [95% CI, -0.16 to 0.41]; difference between groups, 0.42 SDs [95% CI, 0.01-0.82]; $P = .04$), and these changes in fitness mediated some of the effects (small percentage of mediation [approximately 10%-20%]). The effects of exercise were overall consistent across the moderators tested, except for larger improvements in intelligence among boys compared with girls. **Conclusions and Relevance:** In this randomized clinical trial, exercise positively affected intelligence and cognitive flexibility during development among children with overweight or obesity. However, the structural and functional brain changes responsible for these improvements were not identified.

Trial Registration ClinicalTrials.gov Identifier: NCT02295072



Global Changes in Child and Adolescent Physical Activity During the COVID-19 Pandemic: A Systematic Review and Meta-analysis

Neville RD, Lakes KD, Hopkins WG, et al.

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Key Points

Question: To what extent has the COVID-19 pandemic affected the global physical activity levels of children and adolescents? **Findings:** In this systematic review and meta-analysis of 22 international longitudinal studies that included 14,216 children 18 years and younger, pooled estimates revealed a decrease of 17 minutes per day in children's moderate-to-vigorous physical activity from prepandemic to during the COVID-19 pandemic. **Meaning:** Restrictions implemented during the COVID-19 pandemic have affected children's levels of physical activity, particularly moderate-to-vigorous physical activity; children's movement behaviors should be at the forefront of pandemic recovery efforts.

Abstract

Importance: Numerous physical distancing measures were implemented to mitigate the spread of the COVID-19 virus, which could have negatively affected child and adolescent physical activity levels. **Objectives:** To conduct a systematic review and meta-analysis of the literature that used validated measures to document changes in child and adolescent physical activity during the COVID-19 pandemic and to estimate whether changes in physical activity differed between participant-level, contextual, and methodological moderators. **Data Sources:** PubMed, PsycInfo, SPORTDiscus, Web of Science, Scopus, CINAHL, and MEDLINE were searched (from January 1, 2020, to January 1, 2022). A total of 1085 nonduplicate records were retrieved. Study Selection Studies were included if they reported (1) changes in the duration of physical activity at any intensity for children or adolescents (age ≤18 years) comparing before and during the COVID-19 pandemic using validated physical activity measurement tools and were (2) from general population samples, (3) peer-reviewed, and (4) published in English. **Data Extraction and Synthesis:** A total of 126 articles underwent full-text review. Data were analyzed using a random-effects meta-analysis, which was conducted in January 2022. **Main Outcomes and Measures:** Change in the duration of engagement in physical activity at any intensity comparing before and during COVID-19. **Results:** Twenty-two studies including 46 independent samples and 79 effect sizes from 14,216 participants (median age, 10.5 years; range, 3-18 years) were included. The percentage change in the duration of engagement in total daily physical activity from before to during COVID-19 was -20% (90% CI, -34% to -4%). Moderation analyses revealed that changes were larger for higher-intensity activities (-32%; 90% CI, -44% to -16%), corresponding to a 17-minute reduction in children's daily moderate-to-vigorous physical activity levels. The reduction in physical activity was also larger for samples located at higher latitudes (37%; 90% CI, -1% to 89%) and for studies with a longer duration between physical activity assessments (25%; 90% CI, -0.5% to 58%). **Conclusions and Relevance:** Children and adolescents have experienced measurable reductions in physical activity during the COVID-19 pandemic. Findings underscore the need to provide bolstered access to support and resources related to physical activity to ensure good health and social functioning among children and adolescents during pandemic recovery efforts.



Using Time-out for Child Conduct Problems in the Context of Trauma and Adversity: A Nonrandomized Controlled Trial

Roach AC, Lechowicz M, Yiu Y, Mendoza Diaz A, Hawes D, Dadds MR.

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Key Points

Question: Are parenting programs that include time-out less effective or even harmful for children exposed to adverse childhood experiences? **Findings:** In this nonrandomized clinical trial of 205 families, children with conduct problems and high adversity exposure experienced equivalent, if not greater, outcomes, measured by the parent-reported Strengths and Difficulties Questionnaire, after a parenting program that included time-out, compared with children with low adversity exposure. **Meaning:** This study suggests that, despite concerns that time-out is contraindicated for children who have experienced adversity, parenting programs that include time-out appear to be beneficial for children with or without adversity exposure for management of emotional and behavioral difficulties.

Abstract

Importance: Exposure to adverse childhood experiences substantially increases the risk of chronic health problems. Originally designed to treat child conduct problems, parent management training programs have been shown to be effective in preventing children from being exposed to further adversity and supporting children's recovery from adversity; however, there are increasing concerns that a core component of these programs, the discipline strategy time-out, may be harmful for children with a history of exposure to adversity. **Objective:** To investigate the comparative benefits and potential harms to children exposed to adversity that are associated with parenting programs that include time-out. **Design, Setting, and Participants:** This nonrandomized waiting list—controlled

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clinical study was conducted at a specialist clinic for the treatment of conduct problems in Sydney, Australia. The self-referred sample included children with conduct problems and their caregivers. Eligibility was confirmed through clinician-administered interviews. Data were collected between February 14, 2018, and February 1, 2021. **Interventions:** Caregivers participated in a 10-session, social learning—based parent management training program. Caregivers were provided with parenting strategies aimed at encouraging desired behaviors through effective reinforcement and managing misbehavior through consistent limit setting, including the use of time-outs. **Main Outcomes and Measures:** The primary outcome was the parent-reported Strengths and Difficulties Questionnaire score, and secondary outcomes included subscale scores from the clinician-administered Diagnostic Interview Schedule for Children, Adolescents, and Parents. Multi-informant measures of child adversity were collected using the parent-reported Adverse Life Experiences Scale and the clinician-rated Maltreatment Index. **Results:** A total of 205 children were included in analysis (156 in the full intervention and 49 in the control condition; 158 boys [77.1%]; mean [SD] age, 5.6 [1.8] years [range, 2-9 years]). Compared with children with low adversity exposure, children with high adversity exposure showed greater reductions in the Strengths and Difficulties Questionnaire score from baseline (mean difference, 3.46 [95% CI, 1.51-5.41]; $P < .001$) to after treatment (mean difference, 1.49 [95% CI, -0.46 to 3.44]; $P = .13$) and in the internalizing symptom subscale score (baseline mean difference, 1.00 [95% CI, -2.00 to 0.00]; $P = .50$; posttreatment mean difference, 0.06 [95% CI, -0.82 to 0.94]; $P = .90$). No significant differences in the externalizing symptom subscale score were found. **Conclusions and Relevance:** In this nonrandomized clinical study, children with high exposure to adversity experienced equivalent, if not greater, benefits associated with parenting programs that include time-out compared with children with low exposure to adversity. Results suggest that time-out was an effective component of parenting programs for children exposed to adversity.

Trial Registration: anzctr.org.au Identifier: ACTRN12617001472369



Developmental Variability in Autism Across 17 000 Autistic Individuals and 4000 Siblings Without an Autism Diagnosis Comparisons by Cohort, Intellectual Disability, Genetic Etiology, and Age at Diagnosis

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Abstract

Importance: Presence of developmental delays in autism is well established, yet few studies have characterized variability in developmental milestone attainment in this population. **Objective:** To characterize variability in the age at which autistic individuals attain key developmental milestones based on co-occurring intellectual disability (ID), presence of a rare disruptive genetic variant associated with neurodevelopmental disorders (NDD), age at autism diagnosis, and research cohort membership. **Design:** The study team harmonized data from 4 cross-sectional autism cohorts: the Autism Genetics Research Exchange ($n = 3284$; 1997-2015), The Autism Simplex Collection ($n = 694$; 2008-2011), the Simons Simplex Collection ($n = 2753$; 2008-2011), and the Simons Foundation Powering Autism Research for Knowledge ($n = 10\,367$; 2016-present). The last sample further included 4,145 siblings without an autism diagnosis or ID. **Participants:** Convenience sample of 21,243 autistic individuals or their siblings without an autism diagnosis aged 4 to 17 years. **Main Outcomes and Measures:** Parents reported ages at which participants attained key milestones including smiling, sitting upright, crawling, walking, spoon-feeding self, speaking words, speaking phrases, and acquiring bladder and bowel control. A total of 5,295 autistic individuals, and their biological parents, were genetically characterized to identify de novo variants in NDD-associated genes. The study team conducted time-to-event analyses to estimate and compare percentiles in time with milestone attainment across autistic individuals, subgroups of autistic individuals, and the sibling sample. **Results:** Seventeen thousand ninety-eight autistic individuals (mean age, 9.15 years; 80.8% male) compared with 4,145 siblings without autism or ID (mean age, 10.2 years; 50.2% female) showed delays in milestone attainment, with median (IQR) delays ranging from 0.7 (0.3-1.6) to 19.7 (11.4-32.2) months. More severe and more variable delays in autism were associated with the presence of co-occurring ID, carrying an NDD-associated rare genetic variant, and being diagnosed with autism by age 5 years. More severe and more variable delays were also associated with membership in earlier study cohorts, consistent with autism's diagnostic and ascertainment expansion over the last 30 years. **Conclusions and Relevance:** As the largest summary to date of developmental milestone attainment in autism, to our knowledge, this study demonstrates substantial developmental variability across different conditions and provides important context for understanding the phenotypic and etiological heterogeneity of autism.

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At a Crossroads—Reconsidering the Goals of Autism Early Behavioral Intervention From a Neurodiversity Perspective

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The neurodiversity perspective posits that each person has a unique brain and a unique combination of traits and abilities and asserts that many challenges faced by autistic individuals stem from a lack of fit between the characteristics of autistic people and society's expectations and biases. The neurodiversity movement is akin to a civil rights movement. Among its goals are reducing stigma, increasing accessibility, and ensuring that autistic individuals' voices are represented in decisions about autism research, policy, and clinical practice. The neurodiversity movement is having a growing influence on the scientific community, as evidenced in the recent pause in a large autism genetic study based on concerns raised by the autism community.¹ It is also affecting autism practitioners as, increasingly, parents are expressing reservations about enrolling their child in early intervention programs, citing concerns that such programs do not value neurodiversity and, instead, prioritize changing their child's behavior to fit neurotypical norms.



The diagnostic odyssey of autism: a cross-sectional study of 3 age cohorts of children from the 2016–2018 National Survey of Children's Health

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Child and Adolescent Psychiatry and Mental Health, volume 15, Article number: 58 (2021).

PMID: 34629109 PMCID: PMC8504038 doi: 10.1186/s13034-021-00409-y.

Abstract

Background: Autism prevalence has increased rapidly in recent years, however, nationally representative estimates on the ages of first identification and intervention are out of date. Objectives: (1) To estimate the ages at which children with autism receive their first diagnosis, intervention plan, and developmental services; and (2) To evaluate differences in ages at events by birth cohort and sociodemographic characteristics. **Methods:** Using cross-sectional data from the 2016–2018 National Survey of Children's Health (NSCH), we examined associations via linear regression among a sample of 2303 children aged 2–17 years old, who had ever been diagnosed with autism and either (1) ever had a plan for special education or early intervention, or (2) ever received special services to meet developmental needs. Exposures included age cohort, child, household and healthcare provider characteristics. **Results:** Most children in the study sample ($n = 2303$) were over age 6 years, male, of non-Hispanic white race ethnicity and had mild/moderate autism. Mean ages (years) at first diagnosis was 4.56 (SE = 0.13); first plan was 4.43 (SE = 0.11); and first services was 4.10 (SE = 0.11). After adjustment for exposures and survey year, the middle childhood cohort was 18 months older at first intervention ($\beta = 1.49$, 95% CI, 1.18–1.81), and adolescents were 38 months older at first diagnosis ($\beta = 3.16$, 95% CI, 2.72–3.60) compared to those in early childhood. Younger ages at events were observed among: Hispanic/Latinx as compared to white children, those with moderate or severe symptoms as compared to mild symptoms, and children who received their diagnosis from a specialist as compared to psychologists or psychiatrists. **Conclusions:** Children with autism receive their first diagnosis, intervention plans and developmental services at younger ages than they had in the past. Future research is needed to identify the mechanisms for these improvements in early identification and intervention to accelerate additional progress.

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Defining the anatomy of the neonatal lingual frenulum

Mills N, Keough N, Geddes DT, Pransky SM, Mirjalili SA.

Clin Anat. 2019 Sep;32(6):824-835. doi: [10.1002/ca.23410](https://doi.org/10.1002/ca.23410). Epub 2019 Jun 3. PMID: 31116462.

Abstract

The lingual frenulum is recognized as having the potential to limit tongue mobility, which may lead to difficulties with breastfeeding in some infants. There is extensive variation between individuals in the appearance of the lingual frenulum but an ambiguous relationship between frenulum appearance and functional limitation. An increasing number of infants are being diagnosed with ankyloglossia, with growing uncertainty regarding what can be considered “normal” lingual frenulum anatomy. In this study, microdissection of four fresh tissue premature infant cadavers shows that the lingual frenulum is a dynamic, layered structure formed by oral mucosa and the underlying floor of mouth fascia, which is mobilized into a midline fold with tongue elevation and/or retraction. Genioglossus is suspended from the floor of mouth fascia, and in some individuals can be drawn up into the fold of the frenulum. Branches of the lingual nerve are located superficially on the ventral surface of the tongue, immediately beneath the fascia, making them vulnerable to injury during frenotomy procedures. This research challenges the longstanding belief that the lingual frenulum is a midline structure formed by a submucosal “band” or “string” and confirms that the neonatal lingual frenulum structure replicates that recently described in the adult. This article provides an anatomical construct for understanding and describing variability in lingual frenulum morphology and lays the foundation for future research to assess the impact of specific anatomic variants of lingual frenulum morphology on tongue mobility.

Clin. Anat. 32:824-835, 2019. © 2019 The Authors. Clinical Anatomy published by Wiley Periodicals, Inc. on behalf of American Association of Clinical Anatomists.

Keywords: ankyloglossia; fascia; floor of mouth; frenotomy; lingual frenulum; neonatal; neonate; surgery; tongue tie.

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Osteopathic Manipulative Treatment Decreases Hospital Stay and Healthcare Cost in the Neonatal Intensive Care Unit

Roland H, Brown A, Rousselot A, Freeman N, Wieting JM, Bergman S, Mondal D.

Medicines. 2022; 9(10):49. <https://doi.org/10.3390/medicines9100049>.

Abstract

Osteopathic manipulative treatment (OMT) is used in both inpatient and outpatient settings. Evidence suggests that OMT can reduce both patients’ recovery time and the financial cost of their acute medical treatment and rehabilitation. Multiple studies from neonatal intensive care units (NICUs) are presented in this article that demonstrate infants treated with OMT recover faster, are discharged earlier, and have lower healthcare costs than their non-OMT-treated counterparts. Data clearly show that adjunctive OMT facilitates feeding coordination in newborns, such as latching, suckling, swallowing, and breathing, and increases long-term weight gain and maintenance, which reduces hospital length of stay (LOS). Osteopathic techniques, such as soft tissue manipulation, balanced ligamentous tension, myofascial release, and osteopathic cranial manipulation (OCM), can reduce regurgitation, vomiting, milky bilious, or bloody discharge and decrease the need for constipation treatment. OMT can also be effective in reducing the complications of pneumonia in premature babies. Studies show the use of OCM and lymphatic pump technique (LPT) reduces the occurrence of both aspiration and environmentally acquired pneumonia, resulting in significantly lower morbidity and mortality in infants. Based on published findings, it is determined that OMT is clinically effective, cost efficient, a less invasive alternative to surgery, and a less toxic choice to pharmacologic drugs. Therefore, routine incorporation of OMT in the NICU can be of great benefit in infants with multiple disorders. Future OMT research should aim to initiate clinical trial designs that include randomized controlled trials with larger cohorts of infants admitted to the NICU. Furthermore, a streamlined and concerted effort to elucidate the underlying molecular mechanisms associated with the beneficial effects of OMT will aid in understanding the significant value of incorporating OMT into optimal patient care.

Keywords: neonatal intensive care unit; NICU; osteopathic medicine; osteopathic manipulative treatment; hospital stay; healthcare cost.